REMARKS

Claims 43, 44, 47-55, 57, 62, 65, 67-82, 84 and 87-94 presently appear in this case. No claims have been allowed. The official action of March 4, 2004, has now been carefully studied. Reconsideration and allowance are hereby respectfully urged.

Briefly, the present invention relates to technology developed in the laboratory of the present inventors, which is now known in the art as autoimmune neuroprotection. It has been discovered that secondary neuronal degeneration caused by the neurodegenerative effects of an injury, disease, disorder or condition can be reduced if steps are taken to cause T cells activated against an NS-specific antigen which, in its native state, is present at the site of secondary neuronal degeneration, to accumulate at the site of neuronal degeneration. The mere presence of these activated T cells at the site of secondary neurodegeneration causes a cytokine response that has a significant effect in reducing the secondary neuronal degeneration. The present invention is directed to the improvement in which the T cells are activated by Copolymer 1 or a Copolymer 1-related peptide or polypeptide. The preferred method of causing the T cells to accumulate at the site of secondary neurodegeneration is either to administer T cells activated against Copolymer 1 or

Copolymer 1-related peptide or polypeptide, or to administer the Copolymer 1 or a Copolymer 1-related peptide or polypeptide itself in such a way as to cause a T cell response such that T cells become activated against Copolymer 1 or a Copolymer 1-related peptide or polypeptide.

The interview among Examiners Bunner and Kunz and the undersigned attorney on July 14, 2004, is hereby gratefully acknowledged. Prior to the interview, a chart was forwarded to the examiners showing evidence establishing the broad range of proven activity for various indications and various peptides and T cells. A slightly revised copy of this chart is attached hereto. At the interview, the enablement issues were discussed in light of this evidence. Furthermore, the examiners were forwarded a manuscript by two of the present inventors entitled "A Common Vaccine for Fighting Off Neurodegenerative Disorders: Recharging Immunity for Homeostasis", a copy of which is attached hereto. This manuscript explains that the self-perpetuating spread of damage that follows acute injury or occurs independently of primary risk factors in any chronic neurodegenerative disorder is commonly viewed as secondary degeneration, and that the mechanisms that underlie the secondary degeneration are the same, regardless of whether they are secondary to the primary

insult of an injury or the primary risk factors of a chronic neurodegenerative disorder.

As a result of the interview, the examiners agreed to reconsider the restriction requirement, particularly if additional evidence could be provided establishing that the mechanisms that underlie the secondary degeneration are the same for secondary degeneration following acute injury, as well as chronic neurodegenerative diseases. However, the examiners stated that the independent claims would have to specify the manner of causing the T cells to accumulate at the site of neurodegeneration, such as by specifying the two ways of doing so alternatively, i.e., administering Copolymer 1 or administering T cells activated against Copolymer 1. The examiners further agreed to reconsider the objection to the breadth of the term "Copolymer 1" if the definition from claim 46 were inserted into the independent claims. Furthermore, the examiners stated that the enablement objection would be reconsidered if the claims made very clear that the method was for reducing secondary neuronal degeneration that follows neuronal damage caused by an injury or disease. There was also discussion as to why the prior art use of Copolymer 1 to treat multiple sclerosis does not anticipate the present claims.

The arguments presented at the interview will be repeated hereinbelow in the discussion of the various rejections.

In the final rejection of March 4, 2004, the examiner indicated that claims 45, 50-54, 57-60, 64, 70-78, 84-87, and 90-93 remain withdrawn from consideration in view of the restriction requirement. However, as pointed out in the interviews of record in this case, the newly presented evidence establishes that the same mediators are involved in secondary neuronal degeneration, regardless of whether the primary insult is an acute injury or the chronic degeneration of a disease. As further evidence of this conclusion, the examiner's attention is invited to the attached manuscript of Schwartz and Kipnis, as well as the following two attached references:

(1) FRIEDLANDER, R.M. "Apoptosis and Caspases in Neurodegenerative Diseases" *N Engl J Med*, 348:1365-75(2000)

(2) VAJDA, F.J.E. "Neuroprotection and neurodegenerative disease" *J Clin Neurosci*, 9:4-8(2002)

Friedlander is a review that very clearly includes stroke, brain trauma, spinal cord injury, ALS, Parkinson's disease, etc., in the same category of neurodegenerative diseases. Vajda is another review that describes pathological pathways in five different neurodegenerative diseases. It is believed that these reviews confirm the statements in the

Schwartz and Kipnis manuscript that the same factors, i.e, the same mediators, are involved in secondary neuronal degeneration, regardless of whether the primary insult is an acute injury or the chronic degeneration of a disease.

Furthermore, as will be discussed below, it is believed that the objections to the generic claims in this case will be overcome by the present amendment specifying two alternative ways of causing the T cells to accumulate at the site of secondary neurodegeneration. As it is believed that these generic claims will now be considered to be allowable, withdrawal of the restriction requirement would be in order with respect to the species that fall within this genus. Accordingly, reconsideration and withdrawal of the restriction requirement are again respectfully urged.

The examiner has maintained the objection to the title, but has agreed to hold this in abeyance until all other issues are resolved. It is respectfully requested, however, that this requirement be reconsidered and withdrawn if the present amendment is considered to place the case into condition for allowance. The existing title does appropriately describe the invention as presently claimed. If the examiner still wishes to suggest an amendment to the title, it is respectfully requested that the examiner contact

the undersigned by telephone, so that appropriate language can be agreed to in light of the present scope of the claims.

Claims 43, 55, 56, 79, 82 and 83 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 47, 51, 52, 55, 59 and 60 of copending application no. 09/314,161. The examiner states that Copolymer 1 is an NS-specific antigen, and therefore the instant claims of a method of causing T cells activated against Copolymer 1 to accumulate at the site of neuronal degeneration is not patentably distinct over the copending claim in application no. 09/314,161. This rejection is respectfully traversed.

This double patenting rejection appears to be based upon a misunderstanding. Copolymer 1 is not an NS-specific antigen. Copolymer 1 is a random copolymer consisting of four specific amino acid residues. It may mimic MBP, but certainly it cannot be considered to be an NS-specific antigen. Thus, even if the claims of application 09/314,161 were considered to be prior art, the present claims drawn to the use of Copolymer 1 would not be obvious therefrom, as it was totally unexpected that this random copolymer would behave like an NS-specific antigen in remedial autoimmunity.

It should be noted that application 09/314,161 corresponds to PCT publication WO 99/60021, which was

published on November 25, 1999, prior to the effective filing date of the present application. A copy of this PCT publication is attached hereto. As this application is under final and applicant obviously knew about the publication for more than three months, it is too late to submit it on an Information Disclosure Statement. However, it is merely cumulative to application 09/314,161, which has already been applied in a rejection. If the double patenting rejection is withdrawn for the reasons discussed above, then this publication would not be material to patentability, and therefore would not have to be cited on an Information Disclosure Statement. Nevertheless, it is requested that the examiner, under her own initiative, officially make this document of record in this case.

Reconsideration and withdrawal of this provisional obviousness-type double patenting rejection is therefore respectfully urged.

Claims 43, 44, 46-49, 61-63, 65-69, 79, 81, and 88-89 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting, as being unpatentable over claims 8, 11-14, 25, 31, 33-37, 47, 49, 51 and 60-61 of copending application no. 09/765,301.

In view of the fact that the specification of the present application is substantially identical to that of

application no. 09/765,301, and in view of the substantial agreement at the above-mentioned interview that the restriction requirement would be withdrawn from this case, application 09/765,301 will be allowed to become abandoned for failure to respond to the outstanding official action in that case. At that time, this rejection will have been obviated.

Claims 43, 55, 56, 79, 80, 82 and 83 have been provisionally rejected under the judicially created doctrine of obviousness type double patenting as being unpatentable over claims 45, 49, 50, 53, 57 and 58 of copending application no. 09/893,348. The examiner states that the claims of the '348 application and the instant application recite a method of causing T cells activated by Copolymer 1 to accumulate at the site of neuronal degeneration in an individual in need, and that the present claims are not patentably distinct from the claims in said copending '348 application. This rejection is respectfully traversed.

The '348 application is a continuation-in-part of the '161 application discussed above. As with the '161 application, it relates only to use of NS-specific antigens. The examiner is incorrect to state that the claims of the '348 application recite a method of causing T cells activated by Copolymer 1 to accumulate at the site of neuronal degeneration of an individual in need. There is no mention of Copolymer 1

anywhere in the '348 application. The use of Copolymer 1 is totally unobvious and unexpected from the use of NS-specific antigens as disclosed in the '348 application. Thus, the present rejection should be withdrawn on its merits for the same reasons as discussed above with respect to the '161 application and PCT publication WO 99/60021. It should furthermore be noted that the '348 application has now been abandoned in favor of continuation application no. 10/810,653, filed March 29, 2004. To the extent that this rejection would also apply to the '653 application, applicant urges that it be reconsidered and withdrawn for the same reasons as discussed above with respect to the '348 and '161 applications.

Claims 43, 44, 46-49, 55, 56, 61-63, 65-69, 79-83, 88 and 89 have been rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for a method of reducing secondary neuronal degeneration in the CNS to ameliorate the degenerative effects of crush-injured CNS nerve comprising administering to an individual in need thereof a composition consisting of Copolymer 1 wherein the Copolymer 1 reduces secondary neuronal degeneration, does not reasonably provide enablement for a method for reducing neuronal degeneration caused by the neurodegenerative effects of disease, or for reducing secondary neuronal degeneration that follows the primary neuronal damage of an injury in the

central or peripheral nervous system of an individual in need thereof, comprising causing T cells activated by Copolymer 1 to accumulate at the site of neuronal degeneration. The examiner states that the specification does not enable any person skilled in the art to which it pertains to make or use the invention commensurate in scope with these claims. This rejection is respectfully traversed.

As discussed in the above-mentioned interview, the present amendment now clarifies that it is only directed to reducing secondary neuronal degeneration that follows neuronal damage caused by an injury or disease. In this regard, reference is made to the present specification at page 13, lines 11-15, which refers to the protection of nervous system tissue "from secondary degeneration which may follow damage caused by injury or disease of the CNS or PNS." This new language, which is supported by the specification as indicated above, now makes clear that the claims are directed only to a method of reducing secondary neuronal degeneration. Furthermore, the Schwartz and Kipnis manuscript and the Friedlander and Vajda publications, discussed above and attached hereto, establish that the same factors, i.e. the same mediators, are involved in secondary neuronal degeneration, regardless of whether the primary insult is an acute injury or the chronic degeneration of a disease.

Accordingly, the evidence of record that the present invention is operative to ameliorate the secondary neuronal degeneration following crush-injured CNS nerves, as well as the other evidence of record in the present examples about the treatment of secondary neurodegenerative effects caused by intraocular pressure or glutamate toxicity, would lead one of ordinary skill in the art reading the present specification to understand that such secondary neuronal degeneration can be treated, regardless of whether it is secondary to various acute injuries or various chronic neurodegenerative diseases, disorders or conditions. Note also that the examples in the present application establish that both T cells activated against Copolymer 1 and Copolymer 1 itself are active in reducing the secondary neurodegenerative effects following optic crush injury and following glutamate toxicity. See also Kipnis et al, PNAS 97:7446-7451(2000) with respect to the effectiveness of Copolymer 1 activated T cells or Copolymer 1 itself in the treatment of optic crush, and Bakalash et al, Invest Opthamal.Vis.Sci. 44:3374-3381 (2003) with respect to the effect of Copolymer 1 in reducing secondary neuronal degeneration following intraocular pressure (IOP). See also Angelov et al, PNAS 100:4790-4795 (2003) with respect to the treatment of secondary degeneration following facial nerve injury (which is a PNS condition), Kipnis et al, J Neurotrauma

20:559-569 (2003) with respect to the treatment of neurodegeneration following closed head injury, and Schori et al, PNAS 98:3398-3403 (2001) with respect to treatment of secondary neurodegeneration following glutamate toxicity. The examiner's attention is also invited to WO 03/047500, related to the treatment of secondary degeneration following motor neuron diseases. Another copending provisional application has data relating to the treatment of secondary neurodegeneration following Huntington's disease. Copies of the publications discussed above that are not already of record are attached hereto, other than the non-published copending provisional application. All of this evidence confirms applicant's position that the enablement of the present specification with respect to optic crush, IOP and glutamate would be sufficient to convince those of ordinary skill in the art that the present application would be generally applicable to secondary degeneration following either acute injury or chronic neurodegenerative disease, and therefore that the present claims are indeed commensurate in scope with the present claims.

In the interview, the examiners stated that a greater amount of evidence of enablement is necessary for a recitation of a specific disease, and so the examiners suggested the deletion of claims 56, 58, 59, 83, 85 and 86.

Accordingly, these dependent claims have now been deleted in view of the potential allowability of the claims from which they depend. This deletion should not be considered as any kind of concession with respect to enablement with respect thereto, and thus the deletion is made without dedication, disclaimer, abandonment, waiver, forfeiture or estoppel. The examiner's position that the treatment of these specific conditions is not supported by the present specification is duly noted, however, but is obviated by the deletion of these claims.

While the discussion at the interview was directed to the preamble language "a method for reducing secondary neuronal degeneration that follows neuronal damage caused by injury or disease", the presently proposed claims expand "injury or disease" to read "an injury, disease, disorder, or condition". This is being done merely to avoid any confusion as to whether a given indication is truly "a disease". The term "disorder" is supported by the present specification, and it appears, for example, at page 2, line 10; page 4, lines 18, 21 and 26; page 5, line 11; page 44, line 46; page 46, line 25; and page 57, line 22. The term "condition" is supported in the present specification, as it is used, for example, at page 6, line 18; page 14, line 8; page 24, line 17; page 45, lines 14 and 28; page 55, line 24; page 56, lines 1 and 7;

page 57, line 24; and page 93, line 2. Accordingly, this language is supported by the specification and should also be permitted.

The examiner states that the specification does not teach any methods or working examples that indicate T cells activated by Copolymer 1 accumulate at the site of neuronal degeneration in an individual after administration of the Copolymer 1 protein. This statement is not correct. The examiner's attention is invited to the present specification at page 65 under the heading "Cop 1 Reactive T cells Accumulate in both Injured and Non-injured Neuronal Tissues" for proof of this fact.

The examiner states that any references that the applicant wishes for the examiner to review and make of record must be supplied in the form of an Information Disclosure Statement pursuant to 37 C.F.R. §1.98(a)(1). It is respectfully submitted, however, that 37 C.F.R. §1.98(a)(1) applies only to Information Disclosure Statements filed under 37 C.F.R. §1.97 and 37 C.F.R. §1.97 and §1.98 only relate to applicant's duty to disclose information material to patentability under 37 C.F.R. §1.56. The references submitted in the previous response and those attached hereto (other than WO 99/60021) are not being submitted as prior art, as they do not necessarily have dates prior to the effective filing date

of the present application. They are all being submitted as evidence supporting applicant's position with respect to the enablement rejection, and proving the broad operability of the present invention. Applicants have no desire that these documents be listed on the face of the patent, as they are not prior art that is material to patentability. It is sufficient that reference thereto remain in the file history. Applicants are not aware of any rule that states that evidence submitted to support applicants' position with respect to enablement cannot be considered unless submitted on an Information Disclosure Statement pursuant to 37 C.F.R. §1.98(a)(1).

For all of the above reasons, and in view of the amended language of the claims and the additional evidence presented herewith, the present enablement rejection has now been overcome. Reconsideration and withdrawal thereof is therefore respectfully urged.

Claims 43, 44, 46-49, 55, 56, 61, and 79-83 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite and incomplete for omitting essential steps. This rejection is respectfully traversed.

As discussed in the interview, applicant has acceded to the examiner's suggestion that the independent claims recite in the alternative the two disclosed methods of causing T cells activated by Copolymer 1 or a Copolymer 1-related

peptide or polypeptide to accumulate at the site of neuronal degeneration in the individual in need. While the applicant disagrees that the claims were previously indefinite or incomplete, the amendment to the independent claims presented herewith obviates this rejection. Reconsideration and withdrawal of thereof are therefore respectfully urged.

In the course of the interview, the appropriateness of the restriction requirement insofar as restricting to Copolymer 1 as opposed to Copolymer 1-related peptides was discussed. The examiners agreed that the definition of Copolymer 1-related peptide in previously appearing claim 46 sufficiently defined the Copolymer 1-related peptide to permit it to be included in the present claims in view of the apparent allowability of the use of Copolymer 1. Accordingly, the independent claims have been amended to insert this definition of Copolymer 1-related peptide or polypeptide. This is discussed in the present specification in the section beginning on page 32.

In the interview, the examiners questioned why the present claims defined over the admitted prior art in which Copolymer 1 has been used for the treatment of multiple sclerosis. In order to obviate this issue, the independent claims have now been amended so as to exclude multiple

sclerosis as a disease, condition, or disorder, the treatment of which is covered by the present claims.

The present amendment amends the claims substantially in the manner discussed at the interview, and submits the additional information requested by the examiners. Accordingly, it is believed that this amendment places the case into condition for allowance and should be entered, notwithstanding the status of the present application being after final rejection. It is submitted that all of the claims now present in the case clearly define over the references of record and fully comply with 35 U.S.C. §112. Entry of the present amendment, reconsideration, and allowance are therefore earnestly solicited.

Respectfully submitted,

BROWDY AND NEIMARK, P.L.L.C.
Attorneys for Applicant(s)

By _____
Roger L. Browdy
Registration No. 25,618

RLB:jab
Telephone No.: (202) 628-5197
Facsimile No.: (202) 737-3528
G:\BN\B\BENA\Eis-Schwartz13B\pto\AmendmentD.doc